May 10, 1960

Dr. Niels K. Jerne
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Dear Dr. Jerne:

Many thanks for the manuscript of your very thoughtful paper. I found the care needed to assimilate your new terminology well rewarded, and hope it will find wide acceptance. I certainly agree as to the limitations of present language in precise statement, e.g. the confusion of "antigenic" as immunogenic and paratactic.

I do not disagree with the experimental findings of Cohn et al., on the plurality of antibodies produced by one cell. However, so long as this is limited to a small number, viz. 2, I do not see this as a serious blow to the clonal selection theory. Such cells may arise by successive mutation on alternative chromosomes or, in my opinion more likely, by phagocytosis or other interaction between single mutants. Nossal (who is now here) has some circumstantial evidence that bi-producers are at first very rare; Cohn found substantial numbers of them only after prolonged immunization. We are looking into the kinetics. Also, we should look very closely at antibody production by lymphocytes, which may be manifesting some rather different process than the plasmacytic immunity most of us have studied. Is the lymphocyte actively making soluble antibody? (One might have thought not on grounds of its poorly developed ribosomes.) Anyhow, we have to see whether single cells really make <u>several</u> kinds of antibody.

Are you discouraged by the prospect of suppressing the majority of mutant cells? I would expect to.

Burnet's axiom is even stronger than you indicate (or stress) esp. at pp 2 - 3. The idiom is controlled by the genotype, and further by perinatal experience. As you do indicate this argues against a fixed dictionary of xenotypes and as we all agree, and you state verywell, argues for a random origin of the paraxenotype.

I'm afraid to admit replication of protein: this would be a more violent innovation by far than any of the 9 propositions.

Sorry to have missed you so consistently; à rencontrer.

Yours sincerely,

Joshua Lederberg